

RECENT DEVELOPMENTS IN THE SURGERY OF PEPTIC ULCER*

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THE one outstanding development in the surgery of peptic ulcer in the past nine years has been the renewed interest in the use of bilateral vagotomy. Sufficient time has now elapsed to appraise its effectiveness not only alone, but in combination with either gastroenterostomy or subtotal gastrectomy in the therapy of duodenal ulcer, and its value in the treatment of gastrojejunal ulceration. It is the purpose of this communication to consider briefly these problems.

While the surgical mortality has been definitely lowered, the post-operative morbidity minimized, and the follow-up results steadily improved, duodenal ulcer should be considered primarily a medical problem. Cases should not be operated upon unless complications develop against which conservative therapy is of little avail, or its continuation is dangerous. These are acute perforation, persistent pain failing to respond to medical measures, intractable pyloric stenosis, occasionally massive hemorrhage during the acute phase, and cases in which the bleeding has been recurrent. Yet even with these present indications, less than 15 per cent of duodenal ulcers will require operative intervention.

Thorough and careful preoperative preparation is a "sine qua non" if the mortality and postoperative morbidity are to be kept at a minimum. It is basically essential that electrolytic imbalances, dehydration, avitaminosis, hypoproteinemia and anemia be carefully corrected prior to operation. Gastric dilatation with retention and vomiting must be adequately treated by hot gastric lavages and appropriate parenteral fluids, and if in spite of these measures an alkalosis persists, a preliminary jejunostomy for alimentation may become mandatory. While cases of massive hemorrhage are being operated upon at an early period and in

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increasing numbers in many clinics, they are still being conservatively managed on our medical services with the acquiescence of the surgeons. In the past ten years, 1939 to 1948, there were two hundred and twenty-seven proven cases of acutely bleeding duodenal ulcer in which the hemoglobin fell to 60 per cent or lower. None of these patients was treated surgically. There were nine hospital deaths, a mortality of 3.9 per cent. This conservative attitude may be considered too extreme, but it is felt that in the overwhelming majority of cases there is a tendency for hemorrhage to stop spontaneously, and it is extremely difficult to select for operation only those few patients who might otherwise bleed to death. Perhaps patients who are not stabilized by blood transfusions within forty-eight hours after admission should be explored.¹ But by and large, it is extremely doubtful that the resultant surgical mortality would be lower than 4 per cent. However, at present it is our policy to send all cases recovering from an acute hemorrhage to a convalescent home for recuperation for six weeks, and those in whom there has been a history of previous hemorrhages, are urged to return for radical surgery.

The question of the type of operation to be performed for duodenal ulcer has always been controversial. Formerly it was a question of gastroenterostomy or gastric resection, and now, either of these often combined with vagotomy. No one procedure can be categorically applied to all patients. In any given case an operation should be selected which will entail the minimal risk, and will give clinical freedom from symptoms, allow a return to work, and afford the greatest protection against recurrence of ulceration.

These criteria in our experience have been best fulfilled by gastric resection which may be offered with a very low mortality to about 80 per cent of our patients. Almost thirty years have elapsed since this clinic first advocated subtotal gastrectomy of the Billroth 2 type as the procedure of choice for duodenal ulcer instead of gastroenterostomy and the various types of pyloroplasties. At first there was strong opposition to this so-called radical operation, but it was gradually adopted by most surgeons as the increasing incidence of gastrojejunal ulceration following gastroenterostomy became apparent, and the excellent results obtained by subtotal gastrectomy became known.

However, in 1943,² the advisability and desirability of gastric resection was again challenged when bilateral vagotomy alone was revived and advocated as a definitive curative procedure in cases of chronic

duodenal ulcer without obstruction. At first this technically simple operation was enthusiastically received because its operative mortality was extremely low. Division of the vagi which interrupts the psychic phase of gastric secretion undoubtedly lowers the total and free acid secretion, especially during the night, produces hypomotility, eliminates pain, and in many cases causes the ulcer to heal. But, unfortunately, a vagotomy either complete or incomplete, was often followed by a loss of gastric tone with dilatation of the stomach, producing nausea, vomiting and foul eructations. Moreover the ulcer did not always heal, occasionally perforated, and frequently recurred. The eventual universal dissatisfaction following bilateral vagotomy as a sole procedure is evidenced by the fact that it has now been practically abandoned. Even its most ardent proponents who still prefer it to subtotal gastrectomy now routinely combine infradiaphragmatic vagotomy with a drainage procedure, preferably gastroenterostomy. Excellent results have been reported. Grimson³ states that in a group of one hundred and seventy-five patients, the percentage of satisfactory results was 91.3 per cent, moderately satisfactory results, 5.14 per cent, and definitely unsatisfactory results, 3.4 per cent. In Crile's⁴ experience in one hundred and forty patients followed two to four years after vagotomy and gastroenterostomy for duodenal ulcer, 90 per cent have had satisfactory results, 3 per cent are improved, and 7 per cent are classified as failures. The incidence of demonstrable recurrent ulceration was 4.4 per cent.

We have always advocated gastroenterostomy (combining it since 1946, if possible, with infradiaphragmatic vagotomy) in poor risk patients who probably would not stand the extensive surgery demanded by gastric resection. This group includes those who are extremely obese, and many who have severe diabetes or hypertensive cardiovascular disease, as well as some patients over sixty-five years of age, and a few in whom it is felt that for technical reasons, the closure of the duodenum might present unusual hazards.

Since 1946, ninety-eight patients were subjected to gastroenterostomy, and in sixty-nine, vagotomy was added. There were four deaths, due in two to peritonitis, in one to cardiac failure and uremia, and in the fourth to coronary thrombosis. The appreciable mortality following this simple procedure was due to the fact that these patients were primarily poor operative risks. The follow-up on fifty-five cases of gastroenterostomy with vagotomy followed from eight months to six years,

shows forty-six well, four improved, three possible recurrences, and two proven recurrences. In twenty-nine cases of gastroenterostomy alone, there was one proven recurrence.

Subtotal gastrectomy with and without vagotomy for duodenal ulcer still remains our procedure of choice. From January 1, 1946, to January 1, 1952, in a series of 385 consecutive gastrectomies for duodenal ulcer, vagotomy was added in 165 cases. We have combined infradiaphragmatic vagotomy with subtotal gastrectomy, especially in patients who bled with and without pain, and those in whom the pre-operative secretion studies showed an unusually high HCL, two categories of cases in which recurrences are most likely. We were interested to determine whether the addition of vagotomy would affect the immediate mortality and morbidity, and whether the combination of procedures would diminish recurrent ulceration. We divided these patients into two groups; group 1, those treated by subtotal gastrectomy, and group 2, those treated by subtotal gastrectomy with infradiaphragmatic vagotomy.

Approximately one-third of the patients in each group had had one or more episodes of severe bleeding, and a little less than 10 per cent of the patients had had a previous perforation.

Operation was performed whenever possible under spinal anesthesia, supplemented, if necessary, by either inhalation or intravenous anesthetic agents. Through a median epigastric incision, a bilateral infradiaphragmatic vagotomy was first performed. Then two-thirds to three-quarters of the stomach was resected restoring gastrointestinal continuity by an antecolic Hofmeister termino-lateral gastrojejunostomy. The pylorus was removed in all cases.* The duodenal ulcer was excised whenever possible, but there was never any hesitancy in leaving the ulcer in situ if its removal portended possible damage to the pancreas, or injury to the common bile duct. Permitting the ulcer to remain bears no direct relationship to the subsequent gastrojejunal ulcer since in the nine cases in this series in which there was subsequent recurrence, an active ulcer or healed scar was present in all resected specimens. If the duodenal closure was difficult, and dehiscence envisioned as a possibility, the stump was freely drained. In those eleven cases in which a duodenal fistula developed, the secretions were aspirated by continuous suction. Spon-

* There were two cases of prepyloric exclusion performed during this six year period which are not included in this series.

TABLE I—SUMMARY OF FOLLOW-UP RESULTS
(3 mos. to over 6 years)

SATISFACTORY RESULTS	
Group 1 (S.T.G.) (216 of 220 patients)	Group 2 (S.T.G. and I.D.V.) (161 of 165 patients)
191 Well	146*
13 Improved	11
204 (94%)..... Well or Improved.....	157 (96%)*
UNSATISFACTORY RESULTS	
1 Unclassified	4
(Pain—Negative X-rays)	3 Pain or vomiting or dumping (X-rays negative)
	1 Diarrhea
2 Suspected Recurrences	0
(a) Ulcer Type Pain (X-rays negative)	
(b) Mild Hemorrhage (RUQ Pain. X-rays and Gastroscopy negative)	
9 Proved Recurrences	0
SUBSEQUENT DEATHS*—(DUE TO UNRELATED CAUSES)	
1. Cause unknown. 10 mos. later. (Epileptic)	1. Homologous Serum Jaundice. (4 months later)
	1. Coronary Throm- bosis 1 year later.

taneous closure eventually occurred in all.

The incidence of operative shock was negligible in both groups. Postoperatively after the combined operation (group 2), the incidence of pulmonary complications, gastric dilatation, vomiting and diarrhea was greater.

The mortality in this series of three hundred and eighty-five consecutive gastrectomies was 0.5 per cent. There were two deaths in which a postmortem examination disclosed a pulmonary embolism in one, and in the second, an acute pancreatitis involving the body and tail, complicated by hemorrhage, a colonic fistula and generalized peritonitis. The duodenal suture was competent. Both deaths occurred in group 2, but the addition of vagotomy did not contribute to the fatal outcome.

Follow-up results (Table I) obtained in all but six patients, ranged

TABLE II—TEST MEAL STUDIES — 1946 THROUGH 1951

<i>Group 1</i> S.T.G.		<i>Group 2</i> S.T.G. and I.D.V.	
60 (53%)	anacid of	83 (93%)	anacid of
113	tested	89	tested
33 (79%)	anacid of	30 (100%)	anacid of
42	tested	30	tested
	EARLY GRUEL		
	or ALCOHOL		
	(3 or more months)		
11 (58%)	anacid of	41 (98%)	anacid of
19	tested	42	tested
27 (35%)	anacid of	76 (66%)	anacid of
77	tested	115	tested
25 (66%)	anacid of	43 (86%)	anacid of
38	tested	50	tested
	EARLY NIGHT		
	EARLY HISTAMINE		
	LATE HISTAMINE		
	(3 or more months)		

from three months in a few to over six years in others. The majority of the patients are well and economically restored. However some have failed to gain weight. A minimal incidence of the dumping syndrome was seen in both groups. There was a change of bowel habit in group 2, which could be ascribed to vagotomy, and in about 10 per cent of these patients, there was a diarrhea which was disabling in only one case. Gross hemorrhage occurred in eight patients in the subtotal gastrectomy group, and in two of these, pain was also present. One patient complained of severe pain and x-ray revealed a jejunal ulcer. These nine are assumed to have had recurrent disease, ulceration or erosion. X-ray examination or operation confirmed the presence of a gastrojejunal ulcer in five. The percentage of recurrence in group 1 was 4.1 per cent. These failures are a challenge to surgery and present a difficult problem awaiting solution. There is a common denominator in all these recurrent cases, the presence of free HCL, the titre of which is usually high. Any patient with an ulcer diathesis who shows free HCL postoperatively, is a potential candidate for future ulceration. On the other hand, the presence of an achlorhydria is good insurance against further erosion or ulceration of the gastric or jejunal mucosa. Klein,⁵ in 1929, in animal experiments, found that the incidence of achlorhydria following gastric resection, could be increased by partially eliminating the psychic phase of gastric secretion by adding anterior vagotomy. Cases of subtotal gastrectomy with partial anterior vagotomy, were subsequently reported substantiating his contention.⁶

It is interesting to note, in a comparison of test meal studies (Table II), that regardless of the test stimulant or the time after operation, gastrectomy combined with vagotomy produced a higher percentage of patients with achlorhydria than did gastrectomy alone. Moreover in group 2, there have been no recurrences to date. It would appear, therefore, that the increased incidence of achlorhydria following subtotal gastrectomy combined with vagotomy is directly related to the decreased incidence of recurrence.

In the collected series of duodenal ulcer reported by Jordan,⁷ there was very little difference in the follow-up results of the resected cases when compared to those combined with vagotomy. It is probably for this reason that many surgeons performing gastrectomy, prefer to reserve vagotomy for those cases which later develop gastrojejunal ulceration.

Gastrojejunal ulceration, one of the most serious sequelae of surgery for duodenal ulcer, occurs in 15 per cent to 33 per cent of patients after gastroenterostomy, and in from 3 per cent to 8 per cent following subtotal gastrectomy. These patients invariably require corrective surgery in which the mortality is appreciable, the morbidity marked, and further recurrence not infrequent. A group of eighty-one cases was observed from 1940 to 1950; forty-two gastrojejunal ulcers followed gastroenterostomy (group 1) and thirty-one followed subtotal gastrectomy (group 2); and there were eight patients with gastrojejuno-colic fistula, some of which have been previously reported.⁸

These patients had had duodenal ulcer disease from three months to thirty-six years prior to surgery, and the interval of good health between the primary operation and the first evidence of recurrence averaged 5.2 years, but varied between ten days and twenty-four years. The predominating symptom was usually epigastric pain, frequently associated with bleeding, but hemorrhage alone was the presenting symptom in four. The diagnosis was confirmed by x-ray in most cases, and test meals revealed exceedingly high values of free HCL. Many types of operative procedures were performed in these cases. The follow-up results based upon periodic personal examinations of the patients, cover one and a half to eleven years.

Twenty-nine patients who had a subtotal gastrectomy for gastrojejunal ulceration incident to gastroenterostomy, have been followed. Nine of these were combined with vagotomy. Twenty-three have remained well. These are given in Table III. Six of seven patients treated

TABLE III—RESULTS IN GASTROJEJUNAL ULCERS FOLLOWING GASTROENTEROSTOMY

Subtotal Gastrectomy	15 (75%) well
20 Cases	5 (25%) recurrences
Subtotal gastrectomy plus vagotomy	8 (89%) well
9 Cases	1 (11%) recurrence
Bilateral vagotomy alone	4 (67%) well
6 Cases	2 (33%) recurrences

TABLE IV—RESULTS IN GASTROJEJUNAL ULCERS FOLLOWING SUBTOTAL GASTRECTOMY

Resection of ulcer plus additional resection of stomach and jejunum	9 (69%) well*
13 cases	4 (31%) recurrence
Bilateral vagotomy alone	10 (59%) well
17 cases	7 (41%) recurrence

* Combined with infradiaphragmatic vagotomy in 4.

solely by vagotomy were followed from three to four and a half years. There were two recurrences. One was subsequently treated by subtotal gastrectomy and has remained well for three and a half years, and the other has refused further surgery.

These follow-up observations suggest that the best results in gastrojejunal ulcers following gastroenterostomy are offered by subtotal gastrectomy combined with bilateral vagotomy, reserving vagotomy alone for poor risk patients. However, even the combination of vagotomy and subtotal gastrectomy will not always give protection against further recurrence in these cases.

There were thirty-one patients with gastrojejunal ulcers following gastric resection (group 2). Many had had several antecedent procedures such as gastroenterostomy, vagotomy or jejunostomy. In sixteen of these patients, either because of a previous inadequate gastrectomy, or an obstructing ulcer involving the gastroenteric stoma, a further resection of the jejunum and stomach was necessary, and in four, this was combined with an infradiaphragmatic vagotomy. Of thirteen patients surviving a secondary gastric resection, nine have remained well, and four have developed recurrent ulcer (Table IV).

Bilateral supradiaphragmatic vagotomy as a solitary procedure was first performed by us in 1939 in two cases of jejunal ulcer following subtotal gastrectomy.⁹ Since 1940, vagotomy was done on eighteen such patients, half by the transthoracic approach, and half by the abdominal route without mortality. All cases have been followed. One died three months after operation from an unknown cause. Ten have remained well or were markedly improved. Seven were failures. Four patients with active symptoms in whom the insulin test remained positive after bilateral vagotomy, were subjected to a second operation in a further attempt to divide the nerves completely. The subsequent insulin tests still remain positive. There were three patients whose general physical condition was considered so poor that a preliminary jejunostomy for alimentation was performed and later in two, definitive surgery was attempted. One had a vagotomy with a good result. The other was operated upon elsewhere and died postoperatively.

To recapitulate then, the best follow-up results would seem to have been obtained in those cases in which further gastric resection, when indicated, is combined with infradiaphragmatic vagotomy. However in the poor risk patient, vagotomy alone may be the only procedure which may be safely performed.

When group 1 and group 2 are compared, the poorer results obtained in gastrojejunal ulcers following subtotal gastrectomy, are striking. The reason for this may be ascribed to the fact that in group 1 the ulceration followed an inadequate primary operation, gastroenterostomy, whereas in group 2, even the more radical procedure, subtotal gastrectomy, did not protect against recurrence. These patients apparently must represent a more severe form of ulcer disease. In fact a few of them developed recurrence after recurrence despite a multiplicity of operations, including several gastric resections, vagotomy, or both combined, but in all there was always a persistence of free HCL in high concentration. Possibly this unusual type of case should be treated by total gastrectomy.

Gastric ulcer differs from duodenal ulcer in many respects. It is not as frequent, it occurs in an older age group, and it either may undergo carcinomatous transformation, or may be a carcinomatous ulcer primarily. As Palmer¹⁰ has so tersely stated, "there are no diagnostic signs pathognomonic of benignancy; on the other hand there are definite criteria of malignancy." The clinical history, the x-ray findings, the gastroscopic appearance, and the fact that an ulcer seemingly disappears

under medical therapy, does not always eliminate the possibility of malignancy. Furthermore, in some instances, neither the surgeon at the time of operation, nor the pathologist from the macroscopic examination of the resected specimen, can be positive as to the nature of the lesion. For these reasons, if an iota of doubt exists as to the clinical diagnosis, the case should be explored rather than risk further medical treatment during which period, a so-called "ulcer" may progress to the stage of inoperable carcinoma.¹¹

All surgeons now agree that subtotal gastrectomy with radical removal of the lesion is the only logical operation for gastric ulcer. From 1937 to 1952, subtotal gastrectomy was performed for gastric ulcer in one hundred and eighty-six patients. There were seven deaths (3.7 per cent). The follow-up results of resection for benign ulcer are excellent, and recurrences of either gastric or gastrojejunal ulcer are negligible.

However, benign ulcers, juxta-esophageal in position, presented a special problem. They should be approached with caution because a resection here would invariably imply either a total or an esophagogastrectomy. These operations have an appreciable mortality and immediate postoperative morbidity. And symptoms may develop later due either to stenosis at the point of anastomosis, or to a dilated atonic stomach secondary to complete vagotomy. For ulcers of this type, provided there is every good reason to believe they were benign, and we have not been infallible in our judgment, a Madelener procedure has been performed. This is a palliative gastrectomy in which the stomach is resected distal to the ulcer which remains. With the invariable development of a postoperative achlorhydria, the ulcer heals and the symptoms disappear. This procedure was performed in seventeen cases, most of whom were poor risk patients. There was one death in a patient with a bleeding shallow ulcer in which hemorrhage persisted, and another death on the second postoperative day from a cardiac complication. In two, although the ulcer disappeared by x-ray, and a period of well being ensued, carcinoma became evident in one after three years, and in the other after four years, both inoperable at the time of the second exploration. In the last patient who died postoperatively, and in whom a post-mortem examination was obtained, the pathologist felt that the original benign lesion was not related to the carcinoma. On the other hand, in two other patients, a total gastrectomy was successfully performed for

large cardiac lesions which at the time of operation were thought to be malignant, but were proven to be benign on pathologic examination.

In conclusion, we believe at present that subtotal gastrectomy with vagotomy in duodenal ulcer gives excellent clinical results and offers the best insurance against recurrence. Gastroenterostomy preferably with vagotomy has a distinct place in the treatment of the poor risk patient. Patients who develop gastrojejunal ulceration following gastroenterostomy should be treated preferably by subtotal gastrectomy with vagotomy. Cases with ulceration following subtotal gastrectomy should be treated by further gastrectomy, if previously inadequate, but in all instances by infradiaphragmatic vagotomy. Gastric ulcers should always be treated by subtotal gastrectomy except in a juxta-esophageal ulcer in which palliative gastrectomy may be indicated.

However, in the evaluation of any method of therapy for duodenal or jejunal ulcer, one must bear in mind that once a patient has developed a lesion, there is always the potentiality for recurrence regardless of the type of therapy used. Recurrent ulcers have been reported thirty years after corrective surgery so that any definitive statement as to the permanent effect of any given therapeutic measure based upon the results of short term follow-up observation should be viewed with extreme caution.

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